

CLAIMS

We claim:

1. A method of modulating the interaction between CG and the LHR in a subject comprising administering a therapeutically effective amount of an agent which modulates a CG activity;

wherein the agent modulates CG activity by binding to exoloop 1, exoloop 2 or exoloop 3 of the LHR or to the binding domain of CG creating an agent/exodomain or agent/CG complex.

2. The method of claim 1, wherein the CG is hCG.

3. The method of claim 1, wherein the subject is a vertebrate or an invertebrate organism.

4. The method of claim 1, wherein the subject is a canine, a feline, an ovine, a primate, an equine, a porcine, a caprine, a camelid, an avian, a bovine, an amphibian, a fish, or a murine organism.

5. The method of claim 4, wherein the primate organism is a human.

6. The method of claim 5, wherein the human is male.

7. The method of claim 5, wherein the human is female.

8. The method of claim 1, wherein the agent is CG or a biologically active fragment thereof or other natural or synthetic compound.

9. The method of claim 1, wherein the agent blocks CG binding to the LHR by binding to the LHR.

10. The method of claim 1, wherein the agent blocks CG binding to the LHR by binding to the CG.

11. A method of regulating a CG activity in a subject comprising administering a therapeutically effective amount of an agent which modulates CG activity or modulates CG interaction with the LHR at the site of exoloop 1, exoloop 2 or exoloop 3 on the LHR by modulating the interaction of an exoloop 1, exoloop 2 or exoloop 3 motif on the LHR with the CG.

12. A method of treating a gonadotropin hormone related disease or condition in a male subject comprising administering to the subject a therapeutically effective amount of an agent which modulates CG activity or CG interaction with the LHR at the site of exoloop 1, exoloop 2 or exoloop 3 on the LHR.

13. The method of claim 12, wherein the gonadotropin hormone related disease or condition is selected from a group consisting of male pseudohermaphroditism, microphallus, gynecomastia, bilateral anorchia, absence of Leydig's cells, cryptorchidism, Noonan's syndrome and myotonic dystrophy, delayed puberty, precocious puberty, acne and impotence.

14. A method of treating a gonadotropin hormone related disease or condition in a female subject comprising administering to said subject a therapeutically effective amount of an agent which modulates CG activity or CG interaction with the LHR at the site of exoloop 1, exoloop 2 or exoloop 3 on the LHR.

15. The method of claim 14, wherein the gonadotropin hormone related disease or condition is selected from the group consisting of primary and secondary amenorrhea, delayed puberty, precocious puberty, endometriosis, acne, uterine myoma, ovarian and mammary cystic diseases, and breast and gynecological cancers.

16. A method of contraception in a subject comprising administering to a subject an amount of an agent effective at preventing conception, wherein the agent inhibits CG activity or CG interaction with the exoloop 1, exoloop 2 or exoloop 3 domain of the LHR.

17. The method of claim 16, wherein the agent is CG, a biologically active fragment thereof or other synthetic or natural compound.

18. The method of claim 16, wherein the subject is female.

19. The method of claim 16, wherein the subject is male.

20. A method of promoting fertility in a subject comprising administering to a subject an amount of an agent effective at stimulating fertility, wherein the agent stimulates CG activity or CG interaction with the exoloop 1, exoloop 2 or exoloop 3 domain of the LHR.

21. A method of screening for compounds which modulate the interaction between CG and the exoloop 1, exoloop 2 or exoloop 3 domain on the LHR comprising:

- (a) attaching CG or a biologically active polypeptide fragment thereof to a substrate;
- (b) exposing CG or the biologically active polypeptide fragment thereof to an agent; and

(c) determining whether said agent bound to CG or the biologically active polypeptide fragment thereof and further determining whether said agent modulates the interaction between CG and the exoloop 1, exoloop 2 or exoloop 3 domain of the LHR.

22. A compound identified by the method of claim 21.

23. A composition for treating gonadotropin hormone related diseases comprising a pharmaceutically effective amount of a compound which modulates the LHR at the exoloop 1, exoloop 2 or exoloop 3 domain and a pharmaceutically acceptable excipient.

24. The composition of claim 23, wherein the compound is CG or a biologically active fragment thereof or other natural or synthetic compound.

25. The composition of claim 23, wherein the LHR modulating compound is the compound of claim 22.

26. The composition of claim 23, wherein the LHR modulating compound is an agent which binds to CG thereby preventing its interaction with the LHR at the site of the exoloop 1, exoloop 2 or exoloop 3 on the LHR.

27. A composition for treating a gonadotropin hormone related disease comprising a pharmaceutically acceptable amount of an agent which modulates CG activity, wherein the agent is an antibody which binds to CG and thereby prevents CG from interacting with LHR at the exoloop 1, exoloop 2 or exoloop 3 domain.

28. A method of modulating at least one activity of CG comprising administering an effective amount of an agent which modulates at least one activity of CG at the exoloop 1, exoloop 2 or exoloop 3 domain of the LHR.

29. The method of claim 28, wherein the modulated activity is selected from the group consisting of stimulation of progesterone, androgen and estrogen and stimulation of development of the male and female gonads, follicles, placenta, maturation of oocytes and sperm and growth of cells and tissue.

30. A method of identifying binding partners for CG comprising the steps of:

- (a) exposing the protein to a potential binding partner; and
- (b) determining if an exoloop 1, exoloop 2 or exoloop 3 domain of the potential binding partner binds to CG.

31. A method of modulating the interaction between FSH and the FSHR in a subject comprising administering a therapeutically effective amount of an agent which modulates a FSH activity;

wherein the agent modulates the FSH activity by binding to the exoloop 1, exoloop 2 or exoloop 3 of the FSHR or to FSH creating an agent/exodomain or agent/FSH complex.

32. The method of claim 31, wherein the subject is a vertebrate or an invertebrate organism.

33. The method of claim 31, wherein the agent is FSH or a biologically active fragment thereof or other natural or synthetic compound.

34. The method of claim 31, wherein the agent blocks FSH binding to the FSHR by binding to the FSHR.

35. The method of claim 31, wherein the agent blocks FSH binding to the FSHR by binding to the FSH.

36. A method of regulating a FSH activity in a subject comprising administering a therapeutically effective amount of an agent which modulates FSH activity or modulates FSH interaction with the FSHR at the site of exoloop 1, exoloop 2 or exoloop 3 on the FSHR by modulating the interaction of a exoloop 1, exoloop 2 or exoloop 3 on the FSHR with the FSH.

37. A method of treating a gonadotropin hormone related disease or condition in a male subject comprising administering to the subject a therapeutically effective amount of an agent which modulates FSH activity or FSH interaction with the FSHR at the site of exoloop 1, exoloop 2 or exoloop 3 on the FSHR.

38. The method of claim 37, wherein the gonadotropin hormone related disease or condition is selected from a group consisting of male pseudohermaphroditism, microphallus, gynecomastia, bilateral anorchia, absence of Leydig's cells, cryptorchidism, Noonan's syndrome and myotonic dystrophy, delayed puberty, precocious puberty, acne and impotence.

39. A method of treating a gonadotropin hormone related disease or condition in a female subject comprising administering to said subject a therapeutically effective amount of which modulates FSH activity or FSH interaction at the site of exoloop 1, exoloop 2 or exoloop 3 on the FSHR.

40. The method of claim 39, wherein the gonadotropin hormone related disease or condition is selected from the group consisting of primary and secondary amenorrhea, delayed puberty, precocious puberty, endometriosis, acne, uterine myoma, ovarian and mammary cystic diseases, and breast and gynecological cancers.

41. A method of contraception in a subject comprising administering to a subject an amount of an agent effective at preventing conception, wherein the agent inhibits FSH activity or FSH interaction with the exoloop 1, exoloop 2 or exoloop 3 domain of the FSHR.

42. The method of claim 41, wherein the agent is FSH, a biologically active fragment thereof or other synthetic or natural compound.

43. A method of promoting fertility in a subject comprising administering to a subject an amount of an agent effective at stimulating fertility, wherein the agent stimulates FSH activity or FSH interaction with the exoloop 1, exoloop 2 or exoloop 3 domain of the FSHR.

44. A method of screening for compounds which modulate the interaction between FSH and the exoloop 1, exoloop 2 or exoloop 3 domain on the FSHR comprising:

- (a) attaching FSH or a biologically active polypeptide fragment thereof to a substrate;
- (b) exposing FSH or the biologically active polypeptide fragment thereof to an agent; and
- (c) determining whether said agent bound to FSH or the biologically active polypeptide fragment thereof and further determining whether said agent modulates the interaction between FSH and the exoloop 1, exoloop 2 or exoloop 3 domain of the FSHR.

45. A compound identified by the method of claim 44.

46. A composition for treating gonadotropin hormone related diseases comprising a pharmaceutically effective amount of a compound which modulates the FSHR at the exoloop 1, exoloop 2 or exoloop 3 domain and a pharmaceutically acceptable excipient.

47. The composition of claim 46, wherein the compound which modulates the FSHR at the exoloop 1, exoloop 2 or exoloop 3 domain is FSH or a biologically active fragment thereof or other natural or synthetic compound.

48. The composition of claim 46, wherein the FSHR modulating compound is the compound of claim 45.

49. The composition of claim 46, wherein the FSHR modulating compound is an agent which binds to FSH thereby preventing its interaction with the FSHR at the site of exoloop 1, exoloop 2 or exoloop 3 on the FSHR.

50. A composition for treating a gonadotropin hormone related disease comprising a pharmaceutically acceptable amount of an agent which modulated FSH activity, wherein the agent is an antibody which binds to FSH and thereby prevents it from interacting with the FSHR at the exoloop 1, exoloop 2 or exoloop 3 domain.

51. A method of modulating at least one activity of FSH comprising administering an effective amount of an agent which modulates at least one activity of FSH at the exoloop 1, exoloop 2 or exoloop 3 domain of the FSHR.

52. The method of claim 51, wherein the modulated activity is selected from the group consisting of stimulation of progesterone, androgen

and estrogen and stimulation of development of the male and female gonads, follicles, placenta, maturation of oocytes and sperm and growth of cells and tissue.

53. A method of identifying binding partners for FSH comprising the steps of:

- (a) exposing the protein to a potential binding partner; and
- (b) determining if the exoloop 1, exoloop 2 or exoloop 3 domain of the potential binding partner binds to FSH.